

**Amendments to the Specification:**

Please replace the paragraph beginning at page 2, line 16, which starts with "Estrogen regulates the expression" with the following amended paragraph:

Estrogen regulates the expression of many genes by binding to its two known nuclear receptors, ~~ER $\alpha$~~  estrogen receptor alpha (ER $\alpha$ ) and ~~ER $\beta$~~  estrogen receptor beta (ER $\beta$ ). These two receptor types are encoded by distinct genes, and have distinct ligand affinity and tissue distribution (*see, e.g., Kuiper et al., Endocrinology, 138:863-70 (1997)*). The importance of estrogen receptor  $\alpha$  has been demonstrated by the generation of a knock out mouse, called ERKO. Both male and female ERKO mice are sterile and display a variety of phenotypic effects including decreased bone density, defects in their reproductive tissues, and decreased likelihood of oncogene-induced cancer. *See, e.g., Couse et al., Endocr. Rev., 20:358-417 (1999); Korach, Science, 266:1524-7 (1994); Bocchinfuso et al., Cancer Res., 59:1869-76 (1999)*. Mice lacking estrogen receptor  $\beta$  are fertile, but females display decreased ovarian activity, leading to decreased litter sizes. *Krege, et al., Proc. Natl. Acad. Sci. U S A, 95:15677-82 (1998)*. Mice lacking both  $\alpha$  and  $\beta$  receptors are infertile and display an ovarian phenotype that is distinct from that of either receptor knockout alone. *Couse et al., Science, 286:2328-31 (1999)*.

Please replace the paragraph beginning at page 2, line 1, which starts with "Myosins represent a large class" with the following amended paragraph:

Myosins represent a large class of homologous proteins that have been categorized into at least 15 distinct classes. Class II represents conventional myosins, which are two-headed, filament forming proteins that provide the basis for muscle contraction. The remaining classes represent proteins with distinct structures and functions. For example, members of the myosin superfamily are single-headed or two-headed, and contain any number of a variety of structural domains including ATP-binding domains, actin-binding domains, ~~SH3 domains~~ Src-homology 3 domains (SH3 domains), talin domains, MyTH4 domains, and others. Unconventional myosins have been implicated in a large number of intracellular activities, including cell growth and

development, cell movement, organelle movement, protein localization and transport, endo- and exocytosis, phototransduction, hair cell adaptation, signal transduction, and others. *See, e.g., Mermall et al., Science, 279:527-533 (1998).*

Please replace the paragraph beginning at page 6, line 24, which starts with "Figure 11 illustrates" with the following amended paragraph:

Figure 11 illustrates the tissue specific regulation of mMRP gene by estrogen. RT-PCR was performed on total RNA from WT or ERKO liver and brain tissues treated with vehicle (V), 17 $\beta$ -estradiol (E2) and antiestrogen compound (ZK). RNA quantity was controlled by ~~RT-PCR~~ reverse transcriptase-polymerase chain reaction (RT-PCR) on a house-keeping gene (GAPDH) in the same experiments. The MRP gene was differentially regulated, i.e., it is regulated by the estrogen receptor  $\alpha$  in liver and by the estrogen receptor  $\beta$  in brain.